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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/664,165 | 09/17/2003 | Yuji Imaizumi | 0283-0178P | 4193 |

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| EXAMINER | |
|---|---|
| REYES, HECTOR M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1625 | |

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/664,165 | IMAIZUMI ET AL. | |
| | Examiner | Art Unit | |
| | Hector M Reyes | 1625 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *12-23* is/are pending in the application.

4a) Of the above claim(s) *12-16 and 17-22 in part* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-2 in part and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

## Election

Examiner acknowledges Applicant's response to restriction request, wherein Group III was elected together with compound (1), dichlorodehydroabietic acid as the species required for search purposes. Group is drawn to:

III. **Claims 17-20 in part and 21-22 in part, drawn to a method of opening potassium channels comprising administering** NONHETEROCYCLIC **derivatives embraced in** formula II**, classified in multiple classes and multiple subclasses.** This group may be subjected to further restriction. *A single disclosed species is hereby requested for search purpose.*

The said election, dated on 11/19/04 was made with traverse base upon the following arguments:

- All instant claims are link by a single general inventative concept
- All claims are classified in class 514 and not in multiple classes and subclasses
- There is no burden in search all the subject matter present in the claims.

Applicant's arguments have been fully considered and found not persuasive because:

Regarding the allegedly unity of invention, the inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Compounds required to practice the claimed methods are different since each one of them has a substantially different core and substitution of variable groups in any of the

cores does not provide compounds required in any of the other Inventions. For instance compound II and I have different core thus there is not unity of invention between Groups I and II and Groups III and IV. [1]Regarding the structure II, compounds required in elected Groups III and nonelected Group IV, there is a clear lack of unity since the common core in the said compounds is not Applicant's contribution to the prior art, since a preliminary search indicates that there are thousands of compounds disclosing the said core. See for instance compound having a registry number 798557-11-6, disclosed in 1913.

Moreover, each set of compounds embraced by each group has a different structure and reactivity from the others that a reference anticipating one group would not necessarily render the other obvious and to search all the different structurally diverse compounds in a single application would present a serious undue burden to the Examiner. **Thus a given reference anticipating or suggesting one of the above methods would not anticipates or suggest any of the other inventions under the meaning of 35 USC 102 or 35 USC 103.**

Regarding the classification issue, once a particular compound is required in a given method, the classification of the said method is drawn to the classification of the compound, in addition to the classification of the method itself.

Thus, a serious burden in search exists in searching and evaluating all the subject matter included in all claims in a single application.

The requirement is still deemed proper and is therefore made FINAL.

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[1] See preliminary search of the said core wherein the incomplete search (due to the system limit

## Status of The Claims

Claims 1-11 have been cancelled. Claims 12-22 have been subjected to restriction.

New claim 23 has been added. The following Examination is directed to the elected group III, **directed to claims 17-20 in part and 21-22 in part, drawn to a method of opening potassium channels comprising administering NONHETEROCYCLIC derivatives. Since new claim 23 is directed to the elected species it is also incorporated in the elected group.**

Claims 12-16 and non-elected subject matter embraced by claims 17-20 and 21-23 are withdrawn from consideration.

## Information Disclosure Statement

Examiner has considered IDS dated on December 17, 2004. The Examiner also acknowledges Applicant's drawings and Applicant's letter filed on July 20, 2004 wherein it is indicated that the priority documents are forwarded to the Office. However, no copies of the said priority documents were found in the record.

## *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of essential hypertension, tonic

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exceeded) produced a total of 33,592 citations for only 23.0 % of the whole search. Included is Caplus

bladder, airway hyperresponsiveness and ischemic central nervous disorder, does not reasonably provide enablement for:

- Preventing essential hypertension,
- Preventing tonic bladder,
- Preventing airway hyperresponsiveness and
- Preventing ischemic central nervous disorder.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the said determination the following factors have been considered. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph have been described. They are herein discussed in view of the instant invention:

**The nature of the invention**

In claims 17 and 22 Applicants claim a series of methods to treat and/or prevent:

- Essential hypertension
- Tonic bladder
- Airways hyperresponsiveness or
- Ishcemic central nervous system disorder.

While in pages 1 and 2 of the instant specification a connection or nexus for the treatment of the said conditions or disorders and the opening of the calcium activated

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AN 1939:35193, citation for registry number 798557-11-6 disclosed in 1939.

potassium channels is established, the specification is mute regarding the method for preventing the said diseases or conditions.

**The state of the prior art and the predictability or lack thereof in the art**

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat or prevent which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face. Moreover, there is no prior art disclosing the prevention of the said diseases or conditions.

The instant claimed inventions are highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the prevention of the said medical conditions or diseases are highly unpredictable since one skilled in the art would need to carry out experimentation to determine if any of the multiple claimed compounds embraced by formula II are, indeed, active in the prevention of:

Essential hypertension, Tonic bladder, Airways hyperresponsiveness or Ishcemic central nervous system disorder and if as a consequence, the prevention of the said disorders or conditions can be achieved.

Moreover, the specification lacks to show:

- A method to determine the subjects that would certainly suffer from the said conditions or diseases
- A method showing the treatment that the said subjects need to undergo in order to prevent the said conditions or diseases
- Any data showing a follow up of the said subject already treated by a considerable amount of time in order to support the argument that the said subjects are no longer at any risk from suffering from the said diseases or conditions, including possible side effects affecting other organs of the body.

**The level of the skill in the art**

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine:

1) A clear process for identification of all subjects that would suffer any of the said diseases with a high degree of accuracy

3) Subjecting a representative group of the said subjects to the treatment following a clear series of steps (process)

- A process, including the right age, time and conditions for the subject to receive the "effective amount of the said compound" and the proper treatment-time
- 3) Follow up of the treated subjects for a considerable time in order to show that the subjects already treated would never again suffer from any of the multiple diseases embraced in the claims and the secondary effects, if any, originated by the said treatment.

Thus, the specification fails to provide sufficient support for the said prevention methods. Hence, one of skill in the art would have to perform an exhaustive experimentation without any expectative of success in order to practice the claimed invention regarding the said method of prevention.

Applicants is remind that Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be prevented by the as described in the instant claims, with no assurance of success.

The said elements are critical or essential to the practice of the invention, however are not included in the claims and not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Without the proper identification of subjects

that certainly would suffer a given condition or disease, and further identification of conditions of treatment and follow up of the said group of individuals for a long period of time cannot exist a prevention of a given disease.

## ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 17, 18, 19, 20, 21, 22, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-21 and 23 are indefinite because the phrase "A method of opening potassium channels" is indefinite. What exactly does it mean the "opening of the potassium channels? Indeed the said phrase render such claims as **reach through claims** . Are the said claims directed to the treatment of a particular disease or groups of diseases? Are future diseases yet to be related to the "opening of potassium channels" embraced by the said "mechanism of action? Can Applicant claim the treatment of possible future diseases, even before they emerge or are related to the opening of the potassium channels? Applicant is advised that reach-through claims are improper and indefinite.

Claim 22 is indefinite and confusing because it is not clear how the said method can **prevent** the multiple set of diseases in terms of the methodology use to achieve the said prevention. How can certainly be known the subjects that would be suffering from

the said disease? How are they identified? What is the strategy used in order to shown that the said individuals would never again suffer from the said disease?

## Allowable Subject Matter

No prior art disclosing or suggesting a method of treating essential hypertension, tonic bladder, airway hyperresponsiveness and ischemic central nervous disorder using nonheterocyclic derivatives of formula II were found disclosed in the prior art. The closest art of record was found in Singh et al, J. Chem. Soc. Perkins Trans. (1994), pp3349-3352.

Singh discloses a dihydroxyisoprimane derivative as a agonist of Maxi-Potassium channels. The said derivative is not embrace by formula II or suggests derivatives of the said formula.

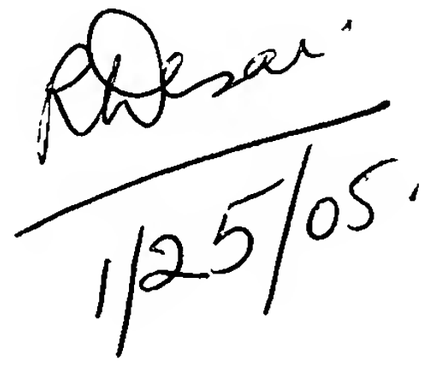
## CONCLUSION

Any inquiry concerning this communication should be directed to Hector M. Reyes whose telephone number is (571) 272-0691. The examiner can normally be reached on Monday to Friday from 9 am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner 's primary, Ms. Rita Desai, which telephone number, is (571) 272-0584 or Examiner's Supervisor Ms. Cecilia Tsang, at (571) 272-0562.

Héctor M. Reyes PhD, JD

Ms. Rita Desai



Art Unit 1625
USPTO Reg. # 54,846
January 25, 2005.

Primary Patent Examiner